REMARKS

Claims 86-92, and 95-101 were pending in the present application. Claims 89, 90, 98 and 99 have been amended. The remarks made herein are designed to place the case in condition for allowance. As such, Applicants respectfully request that the remarks made herein be entered and fully considered.

The Rejection of Claims 89, 90, 98 and 99 under 35 U.S.C. §112, Second Paragraph, Should Be Withdrawn

Claims 89, 90, 98 and 99 were rejected under 35 U.S.C. §112, second paragraph, "[a]s being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention." Specifically, the Examiner states that the claims are "[i]ndefinite for the recitation "antibody binds to amino acid residues 15-423 of SEQ ID NO:417" because it is unclear whether it is meant that the antibody binds to all of the residues 15-423 of SEQ ID NO:417, or binds to a region or some residues within the range of the residues 15-423 of SEQ ID NO:417." Applicants respectfully traverse this rejection, however in the interest of expediting prosecution, and in no way acquiescing to the Examiner's rejection, Applicants have amended claims 89, 90, 98 and 99 to recite that the antibody binds to a polypeptide comprising amino acid residues 34 to 254 or amino acid residues 15-423 of SEQ ID NO:417, thereby rendering the rejection moot.

Therefore, Applicants respectfully request reconsideration and withdrawal of the foregoing 35 U.S.C. §112, second paragraph rejection.

The Rejection of Claims 86, 87, 89, 90, 95, 96, 98 and 99 under 35 U.S.C. §103(a), Should Be Withdrawn

Claims 86, 87, 89, 90, 95, 96, 98 and 99 were rejected under 35 U.S.C §103(a), as being unpatentable over Nakagawa *et al.* (J. Lipid Res., 1995, 36:2212-2218) in view of Campbell, A. (Laboratory Techniques in Biochemistry And Molecular Biology, Volume 13, Chapter 1, pages 1-33, 1984). Specifically, the Examiner states that "Nakagawa discloses a rat lysosomal acid lipase, which amino acid sequence (Figure 2) is about 54% identical to the present SEQ ID NO:417, and comprises amino acids 113-135 (23 residues) of the present SEQ ID NO:417 with 100% sequence identity. Nakagawa does not teach antibodies to the lipase." The Examiner then takes a quote from Campbell stating that it is "customary now for any group working on a

macromolecule to both clone the genes coding for it and make monoclonal antibodies to it (sometimes without a clear objective for their application)." The Examiner then concludes that "[i]t would have been *prima facie* obvious to one of ordinary skill in the art at the time the invention was made to make antibodies specific to Nakagawa's lipase"... and that such antibodies "[w]ould specifically bind to the polypeptide of the instant invention because they share the same sequence/epitope (23 amino acids)."

Applicants respectfully traverse this rejection and submit that, for the reasons discussed below, Nakagawa's lipase does not render the claimed antibodies obvious. First, Nakagawa's rat lipase shares only 54% identity with the full length human TANGO294 lipase of the present invention. Applicants assert that fifty four percent identity between inter-species molecules of the same class is quite low. Such a low percent identity likely leads to very different three dimensional molecules due to differences in folding. Second, Nakagawa *et al.* do not analyze their lipase to identify possible antigenic regions and they don't specifically point to the 23 amino acids identified by the Examiner. In fact, since the TANGO294 lipase of the present invention was not known when Nakagawa *et al.* published, Nakagawa could not have known about this small region of overlapping identity. Third, Nakagawa does not teach nor make any antibodies to their lipase. Therefore, Applicants submit that due to the low percent identity between the two molecules, which likely leads to very different three dimensional molecules, that an antibody generated using the full length rat lipase from Nakagawa would likely not specifically bind to the human TANGO294 lipase of the present invention. Additionally, Applicants submit that since i) the TANGO294 lipase of the invention was not known to Nakagawa; ii) Nakagawa does not make antibodies to their lipase and iii) Nakagawa does not determine antigenic regions of their lipase, it would not have been obvious to one of skill in the art at the time of filing to select the 23 amino acids identified by the Examiner to make antibodies. Therefore, contrary to the Examiner's assertions, it would not have been *prima facie* obvious to one of skill in the art, at the time of filing, to make antibodies to Nakagawa's lipase using the 23 amino acid region identified by the Examiner and due to the low percentage identity between the two molecules, antibodies to Nakagawa's lipase would likely not specifically bind to the TANGO294 lipase of the present invention.

The Examiner combines Nakagawa *et al.* with Campbell and asserts that "[i]t is conventional in the art to generate antibodies following the cloning of a gene, as indicated by Campbell." Applicants respectfully traverse this rejection. Despite the fact that Campbell states

that it is customary to make monoclonal antibodies after having cloned a gene, Campbell also states that it costs (in 1984) minimally 10,000£ to generate a monoclonal antibody. Therefore, Applicants assert that at 10,000£ per antibody, it may be prohibitively expensive to generate monoclonal antibodies for some groups, especially if such antibodies are generated "without a clear objective for their application". In fact, Nakagawa *et al.* did not generate any antibodies to their rat lipase. The claimed methods would therefore not have been obvious to one of skill in the art, at the time the claimed invention was made, despite the combination of Nakagawa *et al.* and Campbell. Reconsideration and withdrawal of the 35 U.S.C §103(a) rejection over claims 86, 87, 89, 90, 95, 96, 98 and 99 is respectfully requested.

The Rejection of Claims 88 and 97 under 35 U.S.C. §103(a), Should Be Withdrawn

Claims 88 and 97 were rejected under 35 U.S.C §103(a), "[a]s being unpatentable over Nakagawa *et al.* (J. Lipid Res., 1995, 36:2212-2218), and in view of Campbell, A. (Laboratory Techniques in Biochemistry And Molecular Biology, Volume 13, Chapter 1, pages 1-33, 1984), as applied to claims 86, 87, 89, 90, 95, 96, 98 and 99 above, and further in view of Sandhu (Critical Reviews in Biotech, 1992, 12(5/6): 437-462, especially pages 449-450)." The Examiner combines Nakagawa and Campbell with Sandhu as Sandhu teaches Fab fragments of antibodies. Applicants respectfully traverse this rejection. For the reasons discussed at length above, Applicants submit that the disclosure of the primary reference, *i.e.,* Nakagawa *et al.,* does not render the claimed antibodies obvious and therefore the combination of Nakagawa *et al.* and Campbell with Sandhu does not remedy the deficiency of the primary reference. Reconsideration and withdrawal of the 35 U.S.C §103(a) rejection over claims 88 and 97 is respectfully requested.

The Rejection of Claims 91, 92, 100 and 101 under 35 U.S.C. §103(a), Should Be Withdrawn

Claims 91, 92, 100 and 101 were rejected under 35 U.S.C §103(a), "[a]s being unpatentable over Nakagawa *et al.* (J. Lipid Res., 1995, 36:2212-2218), and in view of Campbell, A. (Laboratory Techniques in Biochemistry And Molecular Biology, Volume 13, Chapter 1, pages 1-33, 1984), as applied to claims 86, 87, 89, 90, 95, 96, 98 and 99 above, and further in view of Hermanus *et al.*, US 3,654,090." The Examiner combines Nakagawa and

Campbell with Hermanus as "Hermanus teaches a method of making enzyme-labeled antibodies or antigens for the determination of antibodies or antigens." For the reasons discussed at length above, Applicants submit that the disclosure of the primary reference, *i.e.*, Nakagawa *et al.*, does not render the claimed antibodies obvious and therefore the combination of Nakagawa *et al.* and Campbell with Hermanus does not remedy the deficiency of the primary reference. Reconsideration and withdrawal of the 35 U.S.C §103(a) rejection over claims 91, 92, 100 and 101 is respectfully requested.

CONCLUSIONS

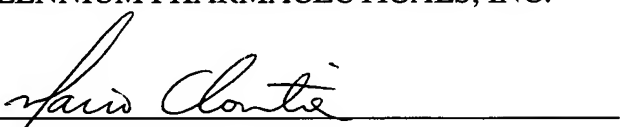
In view of the amendments and remarks made herein, Applicants respectfully submit that the rejections presented by the Examiner are now overcome and that this application is in condition for allowance. If in the opinion of the Examiner, a telephone conference would expedite the prosecution of the subject application, the Examiner is invited to call the undersigned.

It is believed that this paper is being filed timely as a request for a two month extension of time is filed concurrently herewith. No additional extensions of time are required. In the event any additional extensions of time are necessary, the undersigned hereby authorizes the requisite fees to be charged to Deposit Account No. 501668.

Entry of the remarks made herein is respectfully requested.

Respectfully submitted,

February 11, 2008 MILLENNIUM PHARMACEUTICALS, INC.

By 

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